OREGON
HEALTH SCIENCES UNIVERSITY
3181 S.W. Sam Jackson Park Road, L333A, Portland, Oregon 97201-3098 (503) [redacted] FAX 494-8393
494-8414 494-4430
School of Medicine
Department of Biochemistry and Molecular Biology

January 14, 1992

Captain Steven Lewis
Office of Naval Research
Combat Casualty Care Research Area
Naval Medical Research & Development Command
Naval Medical Command, National Capitol Region
Code 405
Bethesda, MD 20814-5044

Subject: Periodic Report for Award N00014-90-J1797
Liquid Collagen Wound Coverings

Dear Captain Lewis:

Attached is a brief summary of research progress since our last report of September 10, 1991.

Yours sincerely,

J. Peter Bentley, PhD
Professor of Biochemistry
and Molecular Biology

cc: Administrative Grants Officer
Director, Naval Research Laboratory
Defense Technical Information Center
Office of Chief of Naval Operations
Bureau of Medicine and Surgery

Liquid Collager Wound Coverings Award Number N00014-90-J1797 Periodic Report
January 14, 1992

Administrative

On December 5, 1991, the laboratory was site visited by David Moran, PhD, from the Office of Technology Assessment at ONR. A verbal progress report was presented to Dr. Moran at that time.

I have been notified that a patent will be issued for the discovery that iodine causes collagen solutions to gel, and thus permits their use as liquid wound dressings. A supplementary patent application for the kit in which the wound covering materials are held in a plastic container for shipment has been filed.

In November I visited the Wound Care Division of Minnesota Mining and Manufacturing Corporation in St. Paul, Minnesota and presented a seminar to them describing the wound covering material and kit. This visit was made at the suggestion of Captain Steven Lewis in an attempt to license the product to a manufacturing company. I have subsequently been informed that, although the product appears to have promise, it does not fit well with the current product line for 3M and they do not wish to pursue the matter further.

Recruitment

The direction taken by the project increasingly requires examination of our materials by light and electron microscopic techniques and we are experiencing difficulty in achieving the right degree of collaboration with investigators at this institution. It is therefore necessary to hire a full time associate with these skills. An ad has been placed in the January 22 edition of *Science* and it is hoped that a morphologist at the level of senior research associate or research assistant professor can be hired to assist with the project.

Freeze Drying of Collagen

The current procedure involves freezing of collagen solutions by dripping the solution into liquid nitrogen and lyophilizing the beads thus generated. This is less than satisfactory, because it is extremely time consuming and the beads tend to compress and are not readily soluble. We have developed a liaison with Oregon Freeze Dry, which is the world's largest processor of freeze dried products (see brochure). This company is interested in expanding the use of freeze dry technology beyond the food industry and is thus interested in collaborating with us. They have freeze dried our collagen preparations at three different rates of freeze in order to vary the size of the ice crystals. As the ice crystals are removed, varying size voids are left in the collagen felt, permitting different rates of rehydration and solubilization. We have determined that a freezing rate of 1° per minute provides optimum rehydration characteristics, which are far better those of our laboratory freeze dried material. We are now packaging freeze dried wound covering material and will make this available to other hospitals.

Human Studies

The preliminary studies were conducted on donor site wounds in patients undergoing plastic or reconstructive surgery in order to demonstrate that the wound covering material was well tolerated, painless, and produced no complications. These studies were conducted successively by Kathleen Waldorf, MD, and Richard Harding, MD, both at this institution. These preliminary studies are now concluded and we now propose to test the materials on more serious burn wounds with the collaboration of Phillip Parshley, MD, Chief of the Oregon Burn Center at Emanuel Hospital in Portland.

Vehicle for Growth Factors

Collagen crosslinked with DOPA has been molded in plastic syringes into firm gelatinous plugs. Platelet derived growth factor has been added to these plugs prior to implantation subcutaneously in rabbits. The plugs have been removed after varying periods in place and are currently being processed for histology.